Assessing agreement between point of care and laboratory results for lipid testing from a clinical perspective

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Abstract

Objectives: Investigate agreement between lipid pathology results from point-of-care testing (PoCT) devices and laboratories.

Design and methods: Agreement was assessed using the Bland–Altman method.

Results: Mean difference (limits of agreement) were: −0.28 mmol/L (−1.04, 0.48) for total cholesterol, −0.09 mmol/L (−0.55, 0.36) for HDL-C. Median difference (nonparametric limits of agreement) were 0.07 mmol/L (−3.04, 3.04) for triglycerides.

Conclusions: The clinical acceptability of the variation between lipid PoCT and laboratory test results is debatable but our work provides baseline data for further research.

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Introduction

Point of care testing (PoCT) which is a test performed on-site at the time of consultation, can facilitate the management of chronic conditions. Before PoCT can be implemented as a safe and effective alternative, acceptable performance compared with laboratory methods from both a clinical and analytical perspective needs to be established [1].

Few studies have assessed the clinical agreement between lipid PoCT results obtained in a general practice (GP) setting compared to laboratory results [2]. The paucity of such comparative data makes it difficult to determine the acceptable difference in results and further research is required. The aim of this study was to assess agreement for clinical decision-making between lipid results obtained from pathology laboratories and Cholestech LDX devices used in the Australian GP setting.

Keywords:
Point of care testing
Lipids
General practice

Materials and methods

Study design and participants

This study was part of the Point of Care Testing in General Practice Trial conducted in 2005–2007. The methodology and rationale for this randomised trial has been reported in detail elsewhere [3].

In this study, 30 practices from urban, rural and remote locations across three states in Australia were provided with a Cholestech LDX PoCT device for measuring lipids. Patients were eligible to participate if they were ≥18 years, had established hyperlipidaemia and were currently taking or had been eligible for lipid lowering medication [4]. Written informed consent was obtained from all practices and patients (n = 2356) participating in the study.

Pathology testing

Over a 6-month period, patients presented for testing according to their usual lipid testing schedule. Testing was performed by the PoCT device in the practice and patients were instructed to have a second test performed on the same day by the laboratory. Seventy percent of practices performed venepuncture at their practice with a large
proportion of these practices using a courier service to transport the blood to a laboratory.

Laboratory testing involved the patient’s venepuncture sample analysed using the laboratory’s routine method by a technician/scientist. Twenty-three laboratories participated in the study, were accredited by the National Association of Testing Authorities and participated in the Royal College of Pathologists of Australasia Quality Assurance Programs external proficiency testing scheme. Eleven of the 23 laboratories provided information on the lipid assays. Four instruments were used: Roche Diagnostics (6), Olympus (2), Ortho Clinical Diagnostics (2) and Siemens Dimension (1).

Ethics

Ethical approval was obtained from five independent Australian Human Research Ethics Committees.

Statistical analysis

Matching of pathology results collected from PoCT devices and laboratory testing was performed by patient, date and type of test. Only dual measurements performed on the same day were included in the analyses. All analyses were performed using SAS version 9.1.3 (Cary, NC, USA).

To assess concordance, frequencies and percentages were calculated for PoCT and laboratory lipid results within and outside therapeutic range. Based on published clinical guidelines [5] test results were classified as within target range if they were ≤4.0 mmol/L for total cholesterol, >1.0 mmol/L for HDL cholesterol (HDL-C) and <2.0 mmol/L for triglycerides. The percentage of dual measurements where the difference did not exceed 20% of the average value was calculated for discordant results. As this analysis concerns comparison of the effect on clinical decision making of

Fig. 1. Bland–Altman plots of PoCT and pathology laboratory test results (— mean, - 95% limits of agreement).
different lipid measurement methods, the choice of therapeutic range is not critical.

To assess agreement, the Bland–Altman analysis [6] for comparing methods with multiple pairs of results per individual was adapted to allow for additional clustering due to patients being nested within practices. Where model assumptions appeared reasonable, a paired t-test with allowance for clustering at the practice and patient levels was used to test whether the bias differed from zero. Results are presented as estimated bias, 95% confidence interval for bias and 95% limits of agreement. Where model assumptions were not met, the nonparametric approach suggested by Bland and Altman [7] was adopted. Median, 2.5th and 97.5th percentiles of the differences are presented. The estimated bias and 95% limits of agreement, or median and percentiles were included on Bland–Altman style plots of the difference in results against the average.

Results

Participants

Of the 2356 patients recruited to the study, 765 were included in the agreement analysis for at least one of total cholesterol, HDL-C and triglycerides. Baseline characteristics of patients included in the analysis are shown in the supplementary materials.

Matching

There were 867, 778 and 864 dual measurements available for analysis for total cholesterol, HDL-C and triglycerides, respectively. The median number of matched tests per person was 1 (range 0-3) for each type of test. The number of patients contributing at least one pair of test results was 763, 699 and 762 for total cholesterol, HDL-C and triglycerides respectively, representing 26 general practices. Medians and interquartile ranges are reported for each type of test (supplementary materials).

Concordance

There was agreement between the PoCT and laboratory test result in relation to whether the result was within target range for 85%, 86% and 89% of dual measurements for total cholesterol, HDL-C and triglycerides respectively. The percentage of discordant dual measurements with a difference that did not exceed 20% of the average result was 92%, 50% and 32% for total cholesterol, HDL-C and triglycerides, respectively.

Agreement

Bland–Altman plots for total cholesterol and HDL-C are shown in Fig. 1. For total cholesterol, the estimated bias was $-0.28 \text{ mmol/L}$ (95% CI $-0.37$ to $-0.20$, $p<0.0001$) and 95% limits of agreement were ($-1.04, 0.48 \text{ mmol/L}$). For HDL-C the estimated bias was $-0.09 \text{ mmol/L}$ (95% CI $-0.15$ to $-0.04$, $p=0.0017$) and the 95% limits of agreement were ($-0.55, 0.36 \text{ mmol/L}$).

A plot of the difference in results versus the average triglyceride concentration suggested that the variance of the differences was not constant throughout the range of measurement (Fig. 2) and the differences were positively skewed. A log transformation of the data did not resolve these issues and thus a nonparametric approach was adopted. The median difference was 0.07 mmol/L and the 2.5th and 97.5th percentiles were $-0.40$ and 2.04 mmol/L respectively.

Discussion

This study assessed agreement between lipid test results obtained using Cholestech LDX PoCT devices in GP and numerous laboratories.

Bland–Altman analysis showed that, on average, PoCT devices underestimated total cholesterol and HDL-C results but overestimated triglyceride results compared to the laboratory. The Bland–Altman plots showed that the variability of the differences was fairly constant throughout the range of measurements for total cholesterol and HDL-C, suggesting that agreement is relatively constant for high and low values. For triglycerides, agreement appears to worsen with increasing values. One possible explanation for the overestimation of triglyceride PoCT results compared to the laboratory is biological variation [8]. Triglycerides can exhibit large within individual variation and, although the study required fasting lipid tests to be performed, this may not have occurred at all times.

Fig. 2. Bland–Altman style plot of PoCT and pathology laboratory test results (--- median, 2.5th and 97.5th percentiles).
High levels of concordance between PoCT and laboratory test results were found for all the tests. Whether this concordance is clinically acceptable is a matter for debate but our study provides data that can help define a clinically acceptable misclassification rate. In terms of clinical acceptability, the accuracy of the test result is a key component to inform the physician about decisions for optimal treatment but is not the only information driving a clinical decision. A patient’s risk for cardiovascular events as well as other patient factors such as adherence to diet are also important in the clinical decision making process. Hence what is an acceptable variation in results for one patient may not be acceptable for another.

There are limitations to our study. First, different laboratory methods were used as the reference point. It was not feasible to have one reference laboratory due to the size of the study and geographic spread of practices. Consequently the potential for greater result variability in our laboratory reference method existed and may have contributed to the wider range of the limits of agreement. This disadvantage is offset by employing normal practice in which a laboratory of the individual GP’s choice is used. The variability of results found in this study is also a better reflection of the reality of everyday practice and the effects of implementing PoCT.

Second, as this was a pragmatic study taking place in busy general practices, the study protocol did not standardise the timing of when the tests had to be performed. This approach may have caused some bias and we acknowledge that biological, intra-individual and analytical variations may have influenced lipid concentrations. However, 70% of practices performed venepuncture in their practice and only dual measurements performed on the same day were included in the analysis. Furthermore, research by Rogers and colleagues [9] reported that the reliability of the Cholestech LDX for total cholesterol outside of a controlled environment required investigation which has been addressed by our study.

Research reporting the comparative agreement between paired PoCT and laboratory lipid test results for monitoring patients with established hyperlipidaemia in GP is scant. We found variation in lipid values between PoCT and laboratory test results. The clinical acceptability of this variation is debatable with further research required.

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Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.clinbiochem.2009.11.014.

References